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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,600	04/01/2002	Alain Aulombard	IVD 1127	6447
27546	7590	10/31/2003	EXAMINER	
SANOFI-SYNTHELABO INC. 9 GREAT VALLEY PARKWAY P.O. BOX 3026 MALVERN, PA 19355			ANDERSON, REBECCA L	
			ART UNIT	PAPER NUMBER
			1626	

DATE MAILED: 10/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/030,600

Applicant(s)

AULOMBARD ET AL.

Examiner

Rebecca L Anderson

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 July 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 2-15 and 19-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 17, 18 and 31 is/are rejected.
- 7) ☒ Claim(s) 1 and 16 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                    | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

Claims 1-34 are currently pending in the instant application. Claims 1-15, 19-30 and 32-34 are withdrawn from further consideration as being drawn to non-elected subject matter. Claims 1 and 16 are objected to as containing non-elected subject matter and claims 17, 18 and 31 are rejected under 35 USC 103.

### ***Election/Restrictions***

Applicant's election with traverse of the products of Group I, claims 17-18 and 31 which are optically active salts of the enantiomerically pure compound of formula (I) with an optically active organic acid and the election of this products process for manufacture, Group II, claims 1 and 16, drawn only to the process for the preparation of the salt of the enantiomerically pure form of formula (I) with optically active organic acids by a), b) and c) wherein the compound of formula (I) thus obtained in racemic form is separated into the enantiomers and the enantiomerically pure compound of formula (I) is converted to one of its optically active salts with an optically active organic acid in the paper filed 30 July 2003 is acknowledged. The traversal is on the ground(s) that claims 2-15 and 32-34 depend either directly or indirectly from claim 1 and therefore claim 1 generically covers the subject matter of claims 2-15 and 32-34 and a complete examination of elected claim 1 would necessarily have to include an examination of the subject matter embraced by claims 2-15 and 32-34. This is not found persuasive for essentially the same reasons as stated in the lack of unity requirement mailed 11 June 2003. The inventions listed as Groups I-XIV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2,

they lack the same or corresponding special technical features which define a contribution over the prior art. The Groups I-XIV lack the same or corresponding special technical features for the following reasons: Under 37 CFR 1.475(a), claims 1-34 contain 10 different technical features. The technical feature of claims 1-18 and 32-34 is the compound of the formula (I). The technical feature of claims 19 is the compound of formula (II). The technical feature of claim 20 is the compound of formula (IV). The technical feature of claims 21-22 is the compound of formula (V). The technical feature of claims 23 and 34 is the compound of formula (VI). The technical feature of claim 25 is the compound of formula (VII). The technical feature of claim 26 is the compound of formula (XIII). The technical feature of claim 27 is the compound of formula (XIV). The technical feature of claim 29 is the compound of formula (XIX). The technical feature of the compound of claim 30 is the compound of formula (XX).

Therefore, groups (I-IX), X, XI, XII, XIII, XIV, XV, XVI, XVII, XVIII do not contain the same technical feature and therefore lack unity of invention. For the groups I-X, under 37 CFR 1.475(a) the products and processes defined in the claims lack a significant structural element qualifying as the special technical feature that defines a contribution over the prior art. The products and processes claimed contain the compound of the formula (I), which does not define a contribution over the prior art (as can be seen by WO 96/23787 and Tetrahedron: Asymmetry, 1998, 9, 3251-3262). The reactants, reagents, and reaction conditions vary extensively and when taken as a whole result in vastly different processes. Accordingly, unity of invention is considered to be lacking and

restriction of the invention in accordance with the rules of unity of invention is considered to be proper. Additionally, the vastness of the claimed subject matter, and the complications in understanding the claimed subject matter imposes a serious burden on any examination of the claimed subject matter.

The requirement is still deemed proper.

### ***Claim Objections***

Claims 1 and 16 are objected to for containing non-elected subject matter, specifically the processes for preparing other than the optically active salt of the enantiomerically pure compound of formula (I) with an optically active organic acid. Claims 1 and 16 drawn solely to the elected subject matter, the process for preparing the elected product, the product of claim 17 would appear allowable over the prior art of record.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 17 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,780,466.

Claims 17 and 31 claim an optically active salt of the enantiomerically pure compound of formula (I) wherein X represents a halogen (claim 17), specifically chlorine or fluorine (claim 31), with optically active organic acids.

**Determining the scope and contents of the prior art**

The prior art of record, US Patent No. 5,780,466 discloses the compounds of formula (II), column 21, line 5, and column 23, lines 30-37 in enantiomerically pure form or in racemic form which are useful in the preparation of the compounds of formula (I), column 2, lines 20-25. The compounds of formula (I) as found in the prior art are useful for therapeutic use in pathological phenomena involving the tachykinin system, such as pain, allergy and inflammation, column 1, lines 14-18. Specific enantiomerically pure compounds of formula (I) of the prior art are found, for example, on columns 116 and 117 in examples 68, 69 and

70. US Patent No. 5,780, 466 discloses the compounds of formula (II) of scheme 3, column 33, line 5 wherein E can be H and A is O-CH<sub>2</sub>-CH<sub>2</sub>-, of line 15, column 47 wherein A is O-CH<sub>2</sub>-CH<sub>2</sub> and E is H, and of preparation 1.5, 2-(3,4-Dichlorophenyl)-2-(2-hydroxyethyl) morpholine, which corresponds to applicants instant compound of formula (I) wherein X is chlorine. Column 47, lines 34-43 discloses that to resolve an intermediate of formula (II) one forms a salt with an optically active acid, for example with (+) or (-) tartaric acid.

**Ascertaining the differences between the prior art and the claims at issue**

The difference between the prior art of record and the instantly claimed invention is that the prior art does not specifically disclose the optically active salt of the enantiomerically pure compound of the formula (I) with an optically active acid as instantly claimed. However, the prior art does disclose the compound of formula (II) as found in applicants instant claims, as formula (I), wherein X is chlorine which can be in the form of an enantiomer or a racemic mixture and can be resolved by formation of a salt with optically active acids, for example with (+) or (-) tartaric acid and discloses the compound of formula (I) in its enantiomerically pure forms, for example, examples 68, 69 and 70, columns 116 and 117

**Resolving the level of ordinary skill in the pertinent art**

Minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to prepare an optically active salt of the enantiomerically pure compound of formula (I) wherein X represents a halogen, specifically chlorine, as instantly claimed when faced with the prior art of

US Patent No. 5,780,466 which discloses enantiomerically pure compounds of the formula (I), such as those of examples 68-70, and discloses the intermediate compound of formula (II), specifically 2-(3,4-Dichlorophenyl)-2-(2-hydroxyethyl) morpholine which can be resolved by formation of a salt with optically active acids, for example, tartaric acid. The motivation would be to prepare enantiomerically pure compounds of the formula (I) of the prior art by preparing enantiomerically pure intermediate compounds of the formula (II) which is done by the formation of a salt with an optically active organic acid, in order to have more compounds of the formula (I) which are useful for the treatment of pathological phenomena involving the tachykinin system.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,780,466 as applied to claims 17 and 31 above, and further in view of US Patent No. 5,616,777. While US Patent No. 5,780,466 discloses or renders obvious optically active salts of the enantiomerically pure compound of formula (I) wherein X is halogen, specifically chlorine or fluorine, with optically active organic acids as instantly claimed, it fails to disclose the specific optically active organic acids of L-(-)- or D-(+)-di-para-toluoyltartaric acid as claimed in claim 18. However, US Patent No. 5,616,777 discloses "chiral acids" which are used to resolve a mixture of diastereomers, with preferences towards L-DTTA (di-p-toluoyl-L-tartaric acid, column 4, line 54) and D-DTTA (di-p-toluoyl-D-tartaric acid, column 4, line 53) (column 5, lines 17-25). Reaction Scheme 1, columns 5 and 6 discloses the use of the "chiral acid" to resolve the diastereomers into salts of the enantiomerically pure compounds with the optically active organic acids or



"chiral acids". While US Patent No. 5,616,777 fails to disclose an optically active salt of the enantiomerically pure compound of formula (I) as instantly claimed with an optically active organic acid, it does disclose that L-DTTA and D-DTTA are preferred "chiral acids" which are resolving agents for resolving diastereomers into enantiomerically pure optically active salts with an optically active organic acid.

Therefore, one of ordinary skill in the art, minus a showing of unobvious results, would be motivated to prepare optically active salts of the enantiomerically pure compound of formula (I) with L-DTTA or D-DTTA as instantly claimed when faced with the primary reference which discloses that optically active organic acids such as tartaric acid are resolving agents which prepare optically active salts of the enantiomerically pure compound of formula (II) with optically active organic acids and further in view of the secondary reference which discloses that L-DTTA and D-DTTA are optically active organic compounds which are useful for resolving racemic mixtures, i.e. they are the "chiral acids". Especially since US Patent No. 5,616,777 discloses that L-DTTA and D-DTTA are preferred as the resolving acids, i.e. the "chiral acids" The motivation would be to prepare more the enantiomerically pure compounds of the formula (I) as found in US Patent No. 5,770,466, for example, examples 68, 69, 70 etc. which is a useful compound for the treatment of pathological phenomena involving the tachykinin system such as pain, allergy and inflammation (column 1, lines 14-18) by resolving more compounds of the formula (II) as found in US

Patent No. 5,780,466 by forming salts with optically active acids, specifically L-DTTA or D-DTTA.

### Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (703) 605-1157. Mrs. Anderson can normally be reached Monday through Friday 7:00AM to 3:30PM.

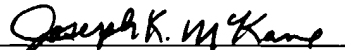
If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone numbers are (703) 308-1235 and (703) 308-0196.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45AM to 4:45PM. The telecopier number for accessing the facsimile machine is (703) 872-9306.



Rebecca Anderson  
Patent Examiner  
Art Unit 1626, Group 1620  
Technology Center 1600



Joseph McKane  
Supervisory Patent Examiner  
Art Unit 1626, Group 1620  
Technology Center 1600